Acanthosis Nigricans among Native Americans: An Indicator of High Diabetes Risk

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ABSTRACT

Prevalence of the skin lesion acanthosis nigricans was determined in two tribal communities in Texas and Nebraska. Thirty-eight percent of the Alabama-Coushatta tribe of Texas had acanthosis nigricans. Nineteen percent of Omaha and Winnebago tribal children had the skin lesion; the youngest children had the least acanthosis nigricans. Among weight-matched Alabama-Coushatta, fasting insulin concentrations were twofold higher in subjects with the lesion. It was concluded that acanthosis nigricans is highly prevalent among Native Americans and that its presence suggests insulin resistance. Thus, it may identify those with the highest risk for non-insulin-dependent diabetes mellitus in this population. (*Am J Public Health.* 1994;84:1839–1842)

Introduction

In the past 40 years, diabetes among Native Americans has changed from a rare occurrence to an epidemic. The prevalence of non-insulin-dependent diabetes mellitus in some tribes is in excess of 50% for those over the age of 35 years.[1,2] In Native Americans, obesity nearly always precedes the development of non-insulin-dependent diabetes.[1]

Acanthosis nigricans, a hyperplastic skin lesion, is associated with insulin resistance and hyperinsulinemia.[3–5] The areas involved include the collar region of the neck, the axillae, the inner surface of the thighs, the elbows and knuckles, and the skin folds of the abdomen. The back of the neck is the most commonly involved and, often, most severely affected area. A previous school-based survey of adolescents found acanthosis nigricans in 0.5% of White children, 5.7% of Hispanic children, and 13.3% of African American children.[5]

We recently performed surveys of two separate Native American communities. These surveys measured the prevalence of obesity and of acanthosis nigricans on the neck in members of the Alabama-Coushatta tribe of eastern Texas and in the children of the Winnebago/Omaha community of northeastern Nebraska. Fasting serum glucose and insulin concentrations were determined in the Alabama-Coushatta subjects.

Research Design and Methods

Acanthosis nigricans is characterized by skin that is thickened, coarse, and darker than the surrounding skin. The presence of acanthosis nigricans was rated as negative (0), mild (1+), moderate (2+ or 3+), or severe (4+), as previously described.[5] Only the neck was systematically examined in all surveys. Obesity was defined as body weight in excess of 120% of ideal weight. Ideal weight was determined from measured height (as defined by the National Diabetes Data Group[6]) for adults and from the normative data of the National Center for Health Statistics for children.[7]

The automated colorimetric method was used in measuring serum glucose concentrations. Serum insulin concentrations were quantitated with a double antibody radioimmunoassay kit (INC-STAR, Stillwater, Minn). Subjects with fasting plasma glucose concentrations greater than 105 mg/dl were asked to return for further testing that included, for most subjects, an oral glucose tolerance test. Diabetes mellitus was diagnosed (1) if at least two fasting plasma glucose concentrations were 140 mg/dl or higher or (2) by the glucose tolerance test criteria of the National Diabetes Data Group.[6]

The Alabama-Coushatta Tribal Council encouraged tribal members to avail themselves of a health evaluation offered by the community health clinic beginning in March 1989. Each family was scheduled for an early morning appointment and asked to arrive after an overnight fast. Over a 1-year period, 260 of the 350 tribal members living on the reservation were examined. This survey was divided chronologically into two phases. The initial 83 subjects received a general examination and only a fasting serum glucose test. These data were included in the analyses of obesity and of the prevalence of non-insulin-dependent diabetes. The subsequent 187 subjects were specifically examined for acanthosis nigricans, and insulin concentrations were also determined. Thirty-three serum samples were lost as a result of improper process-

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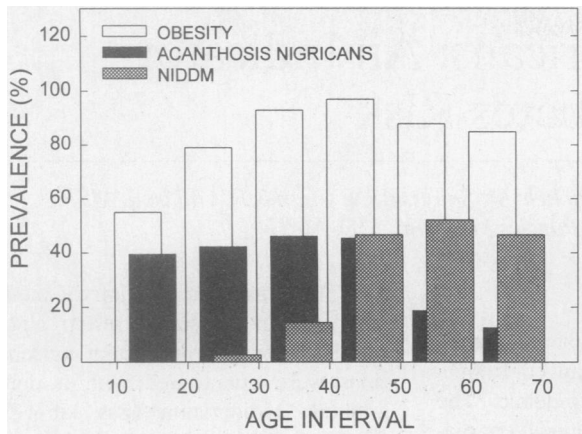
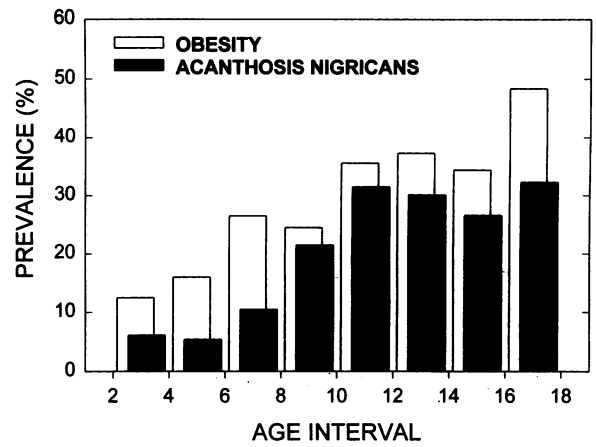
Note. The views expressed in this paper are the authors' and do not necessarily reflect those of the Indian Health Service.



Note. These data are from 260 members of the tribe who were examined over a 1-year period. The numbers of individuals at each age interval were 51, 43, 43, 31, 24, and 27, respectively.

FIGURE 1—The prevalence of obesity, acanthosis nigricans, and non-insulin-dependent diabetes mellitus (NIDDM) among members of the Alabama-Coushatta tribe.



Note. The numbers of individuals at each age interval were 53, 230, 206, 183, 168, 133, 95, and 61, respectively.

FIGURE 2—Age-related prevalence of obesity and acanthosis nigricans among Winnebago/Omaha children.

ing, leaving 144 samples for analysis of insulin concentration.

All of the children of three public schools, one private school, and two community Head Start programs in the Winnebago and Macy areas of northeastern Nebraska underwent screening for obesity and acanthosis nigricans during the fall of 1992. Weight was quantitated on a balance beam scale, and height was measured with a cantilevered sliding measuring scale. Ethnic background was obtained from tribal records. Sixty-eight percent of the Native American children were full blooded, and 92% had at least 50% Native American ancestry. Those having no known Native American ancestors were classified as non–Native Americans. At the time of the survey, five children were not ethnically classified and were excluded from the analysis. No serum samples were collected in this survey.

Fasting insulin concentrations of the Alabama-Coushatta participants were compared between groups with and without the skin lesion by means of two-way analyses of variance.

Results

Prevalence of Obesity and Acanthosis Nigricans

Figure 1 shows the relationship of the prevalence of obesity, acanthosis nigricans, and non-insulin-dependent diabetes to age among 260 members of the Alabama-Coushatta tribe. Among 51 children between 10 and 19 years of age, the prevalence of obesity was 55%. The prevalence of obesity among tribal members in their 40s was 97%. Acanthosis nigricans was identified in each decade of life but had a prevalence of about 40% in the subjects 10 through 49 years old. The prevalence of this skin lesion was lower in subjects greater than 50 years of age, with only about 13% of those in their seventh decade affected. In contrast to the decrease in the prevalence of acanthosis nigricans in later decades, the prevalence of non-insulin-dependent diabetes steadily increased with each decade of life, reaching 52% in the sixth decade.

A total of 1217 children in the Winnebago/Omaha reservations were examined. Seventy-one children were classified as non–Native Americans, and 5 were not ethnically classified. Figure 2 shows the age-related prevalence of obesity and acanthosis nigricans among the 1141 Native American children 3 to 19 years old. Obesity was present in 13% of 53 children less than 4 years old but increased steadily to 37% at 12 years of age. The increasing prevalence of acanthosis nigricans paralleled the prevalence of obesity. Of 1141 Winnebago/Omaha children, 308 (27%) were obese and 219 (19%) had acanthosis nigricans. However, 50 (23%) of those with acanthosis nigricans were not obese. The prevalence of acanthosis nigricans increased with increasing obesity, such that only 7% of Native American children who were 80% to 120% of their ideal weight had the lesion but more than 90% of those who were greater than 180% of their ideal weight had it. In contrast to the Native Americans, age-matched White children in the same community had a lower prevalence of obesity (9 of 71, or 13%) and a much lower prevalence of acanthosis nigricans (only 1 child was affected).

Relationship of Acanthosis Nigricans to Hyperinsulinemia

The relationships between obesity, acanthosis nigricans, and fasting serum insulin levels were evaluated among the Alabama-Coushatta people. Panel A of Figure 3 shows the mean fasting insulin concentrations in members of the Alabama-Coushatta tribe who had at least grade 1 acanthosis nigricans on their necks, obese subjects without acanthosis nigricans, and those who did not have the skin lesion and were within 20% of their ideal weight. Both the obese group and the acanthosis nigricans group had insulin concentrations significantly higher than those of the lean tribal members. Panel B shows similar data from 60 White non-Hispanic subjects grouped by the same criteria. These White subjects were among those evaluated for insulin resistance at the University of Texas Medical Branch General Clinical Research Center for purposes independent of this study. Alabama-Coushatta subjects with acanthosis

nigricans had significantly lower insulin concentrations than did the non-Native Americans with acanthosis nigricans ($P < .01$). In contrast, lean Alabama-Coushatta individuals had significantly higher fasting serum insulin concentrations than did age- and weight-matched White controls (11.2 ± 1.3 vs 6.4 ± 0.7 μU/ml, $P < .01$).

Discussion

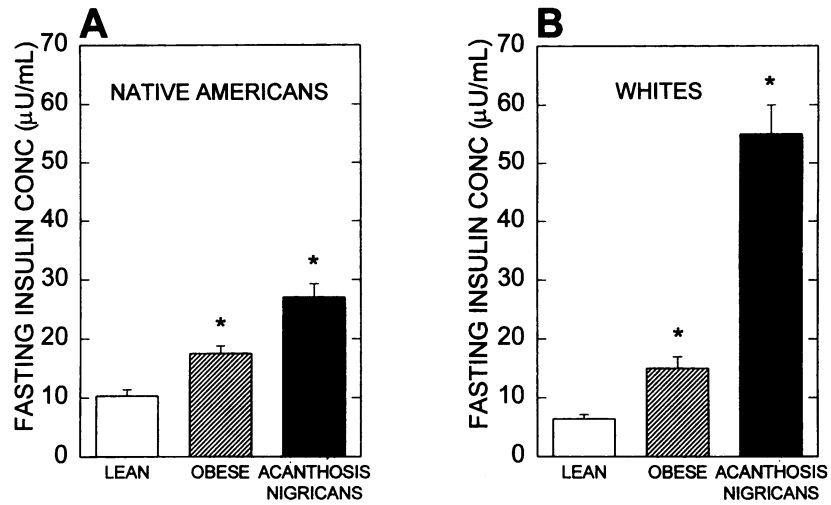
Acanthosis nigricans, a skin lesion once thought to be rare,[8] has recently been established as common, particularly among African Americans and Hispanics.[5] The data presented here demonstrate that this skin lesion is highly prevalent among Native Americans living in two separate areas of the United States. The age of onset of acanthosis nigricans closely paralleled the onset of obesity among Winnebago/Omaha children, with both being present in less than 15% of children under 4 years of age. The prevalences of both obesity and acanthosis nigricans increased steadily during childhood. In children 12 years of age, obesity was present in 37% and acanthosis nigricans in 32%. The prevalence of acanthosis nigricans was far in excess of that seen in our previous school surveys of Whites, Hispanics, and African Americans.[5]

Obesity was present in 55% of 51 Alabama-Coushatta children (10 to 19 years of age). Obesity afflicts virtually everyone among the Alabama-Coushatta people as age advances, and non-insulin-dependent diabetes is present in more than half of the tribal members in their sixth decade of life. The age-related peak prevalence of non-insulin-dependent diabetes was associated with a decline in acanthosis nigricans, which may be a reflection of a decrease in insulin secretion. Nonobese members of the Alabama-Coushatta tribe had significantly higher fasting plasma insulin concentrations than did nonobese White non-Hispanics. This difference in fasting plasma insulin concentrations is consistent with the hypothesis that Native Americans may possess hereditary insulin insensitivity.

Virtually every tribe in the United States and Canada appears to be stricken with a similar epidemic of non-insulin-dependent diabetes.[9–11] Only the Alaskan Eskimos have recently been documented to have a diabetes prevalence no higher than that in the general population of the United States.[12] This excess prevalence of non-insulin-dependent diabetes is not restricted to Native Americans, however; many indigenous peoples across the world have evidenced recent increases in the disease.[13–16]

Hyperinsulinemia is a marker for predisposition to non-insulin-dependent diabetes.[15–23] Hyperinsulinemia, without fasting hyperglycemia, has been found to be a significant risk factor for the development of coronary artery disease in a series of diverse population studies.[18,24–27] The increased risk of coronary disease in patients with insulin resistance may be part of a cluster of hyperinsulinemia-associated characteristics that include high circulating triglyceride concentrations, low plasma high-density lipoprotein, upper body obesity, and hypertension.[19,28–30]

We conclude that the presence of acanthosis nigricans on the necks of Native Americans is a readily visible marker of endogenous hyperinsulinemia and, thus, a marker for risk of developing non-insulin-dependent diabetes. Screening for acanthosis nigricans among Native Americans in clinics and schools to identify individuals at the highest risk for developing non-insulin-dependent diabetes has important implications for developing intervention strategies to combat the diabetes epidemic afflicting Native American communities. □



Note. Panel A shows the means and standard errors for members of the Alabama-Coushatta tribe; panel B contains data from White non-Hispanic subjects. Lean subjects were within 20% of their ideal weight, and obese subjects were defined as those who did not have acanthosis nigricans but were more than 20% above their ideal weight. Asterisks denote concentrations significantly greater than those of lean subjects ($P < .01$). The Alabama-Coushatta groups consisted of 18 lean subjects, 50 obese subjects, and 35 subjects with acanthosis nigricans. The corresponding White non-Hispanic groups consisted of 18, 6, and 36 subjects.

FIGURE 3—Fasting plasma insulin concentrations among subjects with acanthosis nigricans compared with such concentrations among unaffected obese and lean control subjects.

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